P2-165 NSCLC: Combined Modality Therapy Posters, Tue, Sept 4

A phase I/II study of concurrent pemetrexed/cisplatin/radiation in stage IIIa/b non-small cell lung cancer

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Background: Concurrent chemoradiation is the accepted standard of care for most patients with unresectable stage III A/B non-small cell lung cancer (NSCLC) but no standard chemotherapy regimen or schedule has yet been established. Cisplatin, combined with a third generation agent, provides the greatest activity in advanced NSCLC, but to date, no third generation agent has been shown to be tolerable at full dose in combination with radiotherapy (RT) and cisplatin. Pemetrexed/cisplatin (PemC) has shown promising activity in the advanced disease setting and full dose pemetrexed combined with RT or RT/carboplatin has been shown to be safe.

Methods: From December 15, 2005 to December 19, 2006, 10 patients with unresectable stage IIIA/B NSCLC were entered on three dose levels of a phase I trial evaluating PemC combined with 61-66 Gy RT (date of last follow up February 1, 2007). Eligible patients had < 5% weight loss, ECOG PS 0/1, no malignant effusions, FEV1 >1.3 l and adequate organ function. Patients received two q21 day cycles of PemC (Pem 300, 400 or 500 mg/m^2 - day 1, C 25 mg/m^2 days 1-3) concurrent with RT (61 - 66 Gy over 6 to 6.5 weeks) followed by two adjuvant q21 day cycles (Pem 500 mg/m^2 - day 1, C 75 mg/m^2 - day 1). All patients received dexamethasone premedication and B12/folate vitamin supplementation.

Results: Ten patients were accrued (3 at dose levels 1 and 2, 4 at dose level 3). Demographics: median age - 63 years [range 46-69]; stage IIIA/B - 4/6; PS 0/1 - 2/8; median radiation dose - 65 Gy [range 60.5-66]. One patient had dose reduction of cisplatin for cycles 3 and 4 due to elevated creatinine levels, two patients received only cycles one and two (one due to patient refusal despite only grade 2 toxicity having been observed; one in a patient with pre-existing metal allergies who developed progressive cisplatin allergy). Two patients developed grade 4 neutropenia. No grade 3 neutropenia or febrile neutropenia was observed. One patient on dose level 3 required hospital admission for grade 3 esophagitis but was able to complete all planned RT and concurrent chemotherapy. Other grade 3 toxicities were uncommon: hypertension (2); diarrhea (1); anemia (1); hyperglycemia (1); hypophosphatemia (1); thrombocytopenia (1). Partial response (RECIST) has been observed in 7/8 (88%) evaluable patients after independent review with no local progression to date (median f/u 5.3 months). All patients remain alive. One pt has developed distant relapse >12 months after commencing treatment.

Conclusion: Full dose PemC and full dose concurrent RT is well tolerated and preliminary efficacy appears promising. The study is ongoing and has been amended to add a fourth dose level increasing the dose intensity of cisplatin during RT to 20 mg/m^2 daily x 5. A phase II study is planned.

P2-166 NSCLC: Combined Modality Therapy Posters, Tue, Sept 4

Full dose chemoradiation followed by surgical resection in locally advanced NSCLC

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Background: To evaluate the treatment results and toxicities for lung cancer patients treated with trimodality therapy including preoperative concurrent chemotherapy (CT) with high dose radiotherapy (RT) (>60Gy).

Methods: Patients diagnosed with lung cancer between 8/04 and 9/06 and treated with concurrent CT and high dose RT preoperatively at the DFCI/BWH were reviewed retrospectively with IRB approval. Complications and follow up data were recorded. Survival was calculated from the date of diagnosis using the Kaplan-Meier method.

Results: 16 patients were evaluated. The median age was 58 (40-76). Fifteen had NSCLC patients were stage III (8 stage IIIA, 6 stage IIIB), 1 was stage II, one patient had limited stage SCLC with residual disease after chemoradiotherapy. All of the patients completed induction chemoradiotherapy (CRT). CT consisted of weekly carboplatin and paclitaxel for 5 patients (31%) or cisplatin and etoposide q3 wks for 11 patients (69%). Median RT dose was 68 Gy (range: 60-70 Gy). The patients had their surgery at a median of 6.5 weeks (4-16 weeks) after the completion of RT. Pneumonectomy was performed in 2 patients, lobectomy in 10 patients, bilobectomy in 2 patients, lingular resection in 1 patient and wedge resection in 1 patient. Two patients had pCR. Interestingly, 12/16 patients had residual disease at the primary site at the time of resection. In addition, one patient was found to have metastatic satellite nodule in a different lobe, which was surgically removed. Nodal downstaging was present in 12 (75%) of the patients. Two patients had postop empyema and 3 of them had ipsilateral vocal cord paralysis. One of the patients who had empyema had a prolonged hospitalization because of respiratory failure. There were two cases of Gr 3 or greater esophagitis after CRT, one of them requiring dilation. Five of the patients received consolidation chemotherapy with different CT regimens for 2-3 cycles. Median follow up was 12.5 months (6-30). There were 2 local recurrences; both of them were 6 months after surgery. 1 and 2 year local recurrence free survival rate is 90 and 77% respectively. Three patients had distant relapse where 2 of them were local relapsed patients. One and 2 year distant disease free survival rate is 83 and 70% respectively. Overall survival is 100% for 1 and 2 years.

Conclusion: Preoperative high dose RT with concurrent CT is a feasible approach in inoperable lung cancer with acceptable complication and excellent survival rates when done with experienced multidisciplinary team.